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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,582	05/23/2007	Claude LeLouarn	58767.000016	3374

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EXAMINER	
FLOOD, MICHELE C	

ART UNIT	PAPER NUMBER
1655	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,582	LELOUARN, CLAUDE	
	Examiner	Art Unit	
	MICHELE FLOOD	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 15, 2009 has been entered.

Acknowledgment is made of Applicant's cancellation of Claims 2-10 and the addition of newly submitted Clams 11 and 12.

Any rejection not repeated from the previous Office action mail dated December 28, 2008 is hereby withdrawn.

Claims 1, 11 and 12 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1, as amended, and Claims 11 and 12 is/are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the

application was filed, had possession of the claimed invention. The claims are rejected for failing to provide prior support or antecedent basis for the language "comprising administering botulinum toxin type A to the upper lip of said patient [patient suffering from hirsutism] in a quantity sufficient to reduce downy hair growth in said patient" in Claim 1. Newly applied as necessitated by amendment.

Claim 1, as filed in the amendment on May 15, 2009, now recites "A method for reducing hair growth in a patient suffering from hirsutism comprising administering botulinum toxin type A to the upper lip of the patent in a quantity sufficient to reduce downy hair growth in said patient".

However, the specification as originally filed provides only for a method of reducing downy hair growth in a patient in want thereof comprising administering an effective amount of botulinum toxin A to the upper lip of the patient. Nowhere in the specification as originally filed does Applicant disclose a method for the reduction of hair growth in a patient suffering from hirsutism comprising administering the claim-designated ingredient to the upper lip of a hirsute patient in a quantity sufficient to reduce downy hair growth in the patient. While it was indicated in the previous Office action that it appeared that Applicant disclosed a method of treating or reducing hair growth in a patient suffering hirsutism comprising administering an effective amount of botulinum toxin A to said person in need thereof, it was not meant to direct Applicant to amend the claims to introduce new matter into the claimed subject matter. Furthermore, a close review of the specification on page 4, under "Example" discloses:

"A patient of 39 years of age Wants to reduce the downy hairs on their upper lip. A solution containing 3 units of Botox® (a product marketed by Allergan France; the

solution is prepared according to the manufacturer's instructions) is injected into the epidermis of this patient, at several points situated just above the red of their upper lip, the 3 units being spread evenly over the treated area. In the follow-up, 4 months later, the patient clearly presents less downy hair on the upper lip."

Applicant was not intentionally misguided. On page 2, lines 1-4, Cedars-Sinai Medical Center (X) teaches, "Hirsutism is excessive terminal type hair. It needs to be distinguished from "vellus hypertrichosis". This is an excessive growth of vellus-type hair. It may be darker than usual. This is very common in women of Mediterranean descent. It usually runs in families. This is not hirsutism." Also, *see* The Free Dictionary (W**) which describes vellus hair as 'downy hairs'.

Insertion of the above mentioned claim limitation has no support in the as-filed specification. The insertion of the limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the aforementioned broadened concept. There is only one exemplified method for reducing hair growth in a patient comprising administering botulinum toxin type A to the upper lip of a patient in a quantity sufficient to reduce downy hair in the patient, wherein said patient is a patient in want of reducing downy hair growth present on the patient's upper lip. This is not sufficient support for the new genus. This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of

the above mentioned claim limitation is considered to be the insertion of new matter for the above reasons.

As the above mentioned claim limitation could not be found in the present specification, the recitation of the claim limitation is deemed new matter; and, therefore it must be omitted from the claim language, unless Applicant can particularly point to the specification for literal support.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1, as amended, is rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan (A*) in view of Andreyko et al. (U). Newly applied as necessitated by amendment.

Applicant claims a method for reducing hair growth in a patient suffering from hirsutism comprising administering botulinum toxin type A to the upper lip of the patent in a quantity sufficient to reduce downy hair growth in the patient.

Donovan teaches a method of treating a gonadotrophin-related illness in a mammal comprising administering an effective amount of an agent which comprises a light chain component or a fragment thereof a botulinum toxin; a translocation component comprising a heavy chain or a modified heavy chain of a botulinum toxin; and a targeting component which selectively binds to a GnRH receptor. At [0086], Donovan uses botulinum toxin type A to prepare a LHN-GnRH found to be useful in reducing the level of circulating testosterone in a patient; and, reducing the level of circulating gonadotrophin in a patient suffering from precocious puberty with uncharacteristic hair growth (*See* [0132].). Routes of administering the composition taught by Donovan to inhibit secretion of gonadotrophins include direct or local administration of the pharmaceutical at or to the vicinity within an animal body to provide a therapeutic effect (*See* [0053].); and, transdermal, subcutaneous, intramuscular, and intravenous, *etc*. (*See* [0113].). At [0009], Donovan teaches that GnRH agonists and antagonists have been shown to have possible utility in the treatment of hirsutism. The reference does not specifically teach using this product to reduce downy hair growth in a patient suffering from hirsutism.

Andreyko teaches, “GnRH analogs inhibit the secretion of gonadotrophins and, therefore, that of estrogens and androgens of ovarian origin. The purpose of this study was to investigate the use of one superactive agonistic GnRH analog, nafarelin, in the

treatment of hirsutism. Six hirsute women were treated with nafarelin (1000 μg/day) for 6 months. An acute rise in serum gonadotrophin levels occurred in response to nafarelin administration initially, but it lasted less than 2 weeks. Serum gonadotropin, testosterone, free testosterone, and androstenedione concentrations decreased significantly during treatment. Mean serum LH levels decreased from 17.9 ± 4.6 (±SE) to 5.0 ± 0.5 mIU/ml ($P < 0.01$), and FSH decreased from 9.3 ± 0.7 to 7.2 ± 0.9 mIU/ml ($P < 0.05$) after 1 month of treatment. The total testosterone concentration fell from 0.77 ± 0.10 to 0.40 ± 0.14 ng/ml ($P < 0.01$) after 1 month of therapy, and free testosterone decreased from 10.7 ± 2.7 to 4.1 ± 1.6 pg/ml ($P < 0.01$) after 3 months. Androstenedione levels decreased from 2.4 ± 0.4 to 1.2 ± 0.2 ng/ml ($P < 0.01$) after 1 month of treatment. The mean concentrations of all of the above hormones remained suppressed throughout treatment. Serum 5α-androstane-3α,17β-diol glucuronide levels did not decrease significantly during treatment, nor did dehydroepiandrosterone sulfate levels. The mean estradiol concentration during treatment was 34.8 ±3.1 pg/ml. The clinical response was very good; hair growth was slower, and new hair was less coarse compared to the pretreatment period. Hirsutism scores (determined by Ferriman-Gallwey assessment of extent and quality of body hair) improved in four of the six patients. In the six patients, the mean score decreased significantly from 19.3 ± 3.3 to 13.2 ± 2.8 ($P < 0.05$) at the end of treatment. These data demonstrate that by suppressing ovarian androgen production, nafarelin may be useful for the treatment of hirsutism associated with either increased ovarian androgen production or increased sensitivity of the hair follicle to normal concentrations of circulating androgens."

Thus, it was known in the art at the time of the invention that compositions comprising agonistic GnRH analogs which inhibit the secretion of gonadotrophins, are useful in improving the appearance of hair and reducing the growth of hair in patients suffering from hirsutism. Since administration of effective amounts of the agonistic GnRH analog of Andreyko yielded beneficial results in reducing hair growth and levels of serum gonadotrophins and androgen in patients suffering hirsutism; and, since administration of effective amounts of the Donovan' product yielded beneficial results in reducing levels of serum gonadotrophins and androgens in patients; the artisan of ordinary skill in the art would have had a reasonable expectation that using the botulinum toxin type A/GnRH analog product of Donovan to reduce the hair growth in a hirsute patient would be a success. This reasonable expectation of success would have motivated the artisan to administer effective amounts of the Donovan' product to a patient suffering from hirsutism to provide the instantly claimed method because each of the prior art products were shown to inhibit the secretion of gonadotrophins; and, therefore suppress androgen production well known in the art to contribute to the pathogenesis of hirsutism and its characteristic development of excess hair growth and virilization of vellus hairs (also known in the art as 'downy hairs') into unwanted terminal hair growth on the body of hirsute patients, including the upper lip. *See* Jelovsek (V**) and The Free Dictionary (W**), for instance.

The combined teachings of Donovan and Andreyko do not specifically teach administering the product of Donovan to the upper lip of a hirsute patient. However, Donovan does teach that the body site to which the product is administered and the

route of administration of the agent can be varied. Thus, the reference recognizes that the route of administration, as well as the site of the body to which this ingredient is administered can be modified. Therefore, it would have been customary for an artisan of ordinary skill to determine the optimal route and site of administration to best achieve the desired results. Moreover, the adjustment of particular conventional working conditions (*e.g.,* determining a result-effective means for delivering therapeutic products for the treatment of disease conditions) is deemed merely a matter of judicious selection and routine optimization which would have been well within the purview of either one of ordinary skill in the art or the skilled artisan at the time the invention was made.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claims 1, as amended, and newly submitted Claims 11 and 12 is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan (A*) and Andreyko et al. (U) in view of Cedars-Sinai Medical Center (X). Newly applied as necessitated by amendment.

Applicant's claimed invention of Claim 1 was set forth above. Applicant further claims the method for reducing hair growth of claim 1, wherein the method comprises shaving the patient prior to administering the botulinum toxin. Applicant further claims the method for reducing hair growth of claim 12, wherein the method comprises shaving the upper lip of the patient prior to administering the botulinum toxin.

The combined teachings of Donovan and Andreyko are set forth above. The combined references teach the instantly claimed invention except for shaving the patient prior to administering the botulinum toxin; and except for shaving the upper lip of the patient prior to administering the botulinum toxin. However, it would have been obvious to one of ordinary skill in the art to add either of the claim-designated process steps to the method taught by the combined references to provide the claimed method of treatment because at the time of the invention Cedars-Sinai Medical Center taught that anti-androgen therapy for treating hirsutism may be accompanied with shaving of unwanted hair. *See* page 3, fourth paragraph. While, Cedars-Sinai Medical Center does not specifically teach shaving prior to a hormonal therapy for treating hirsutism, Cedars-Sinai Medical Center does teach, "Androgens cause hair to change from vellus to terminal hair. Once a vellus hair has been changed to the coarser terminal hair, it cannot change back." *See* page 1, last line two lines of paragraph 4. Given that it is well known in the art that vellus hair (which differs from hair found on the scalp and androgenic hair) is found on the body of most people; and, given that Cedars-Sinai Medical Center taught that androgens affect hair growth; and, given that Cedars-Sinai Medical Center taught that excessive androgen production contributes to the excessive hair growth and virilization of vellus hair to terminal hair characterizing hirsutism; and, given that Cedars-Sinai Medical Center suggested that shaving should accompany anti-androgen hormonal therapy, the artisan of ordinary skill in the art would have been motivated and would have had a reasonable expectation that modification of the method taught by the combined references as disclosed by Applicant would be a success

because it would have been highly predictable that shaving a patient suffering from hirsutism prior to administration of an anti-androgen agent would beneficially remove hair at different stages of hair growth, as well as any vellus or 'downy hair' which could be affected by circulating androgens present in the serum of the hirsute patient; and, therefore, would provide for a longer lasting result-effect variable for reduced hair growth or reduced hair re-growth and frequency of therapy.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

* Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources. Should you receive inquiries about the use of the Office's PAIR system, applicants may be referred to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

**This reference is cited merely to relay an intrinsic property and is not used herein on the basis for rejection *per se*.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE FLOOD whose telephone number is (571)272-0964. The examiner can normally be reached on 7:00 am - 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele Flood
Primary Examiner
Art Unit 1655

MCF
August 3.2009

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